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Pediatric Tuberculosis Inpatients: Diagnostic Challenges and Short-term Outcomes in a Tertiary Referral Center

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ABSTRACT

Introduction: Tuberculosis (TB) remains a major pediatric health challenge in hospital settings, with significant diagnostic and treatment difficulties. Pediatric TB outcomes are highly variable, with well-established determinants including age, nutritional status, HIV co-infection, and delayed or limited access to care. **Methods**: We conducted a retrospective cohort study of children hospitalized with TB in the Pediatric Infectious Diseases Ward, Children's Medical Center, Tehran, Iran, from January 2016 to December 2021. Data included demographics, clinical presentation, radiologic findings, diagnostic tests, treatment regimens, and outcomes. Not all diagnostic tests were performed in every patient; positivity rates were calculated only among patients who were tested for each diagnostic modality. Associations with in-hospital mortality were analyzed using Fisher's exact test. **Results:** Thirty patients were included (mean age 8.8 ± 3.8 years; 53.3% girls). Of these, 22 (73.3%) were Iranian and 8 (26.7%) were non-Iranian (migrant/refugee). Pulmonary TB was most common (66.7%). Cough (46.7%) was the most common presenting symptom, followed by fever (40.0%) and dyspnea (13.3%). Consolidation/infiltrate (33.3%) and pleural effusion (23.3%) were the main radiographic findings. Among diagnostic tests, the Tuberculin Skin Test (TST) was positive in 19/23 (82.6%), culture in 14/19 (73.7%), PCR in 18/26 (69.2%), and interferon-γ release assay (IGRA) in 5/19 (26.3%). Overall, 27/30 (90%) recovered, while 3/30 (10%) died; fatalities occurred exclusively in patients with central nervous system (CNS) TB or severe pleural disease. Mortality was not significantly associated with age, sex, residence, TB site, or nationality (all $P > 0.05$). **Conclusion**: Pediatric TB often presents with nonspecific symptoms, leading to delayed diagnosis. Among diagnostic tools, TST showed the highest positivity rate, but PCR and mycobacterial culture provided the most consistent and clinically relevant confirmation of pediatric TB, whereas IGRA showed limited utility in this cohort. Most children recovered with standard therapy, but mortality clustered in CNS and severe pleural TB. Strengthening early diagnosis and ensuring equitable access to care—especially for migrant children—remain priorities.

INTRODUCTION

Tuberculosis (TB), a disease caused by *Mycobacterium tuberculosis*, remains one of the most serious health issues affecting children globally. While most infections remain latent, progression to active disease—especially pulmonary TB—occurs more frequently in high-risk pediatric populations [1]. According to the World Health Organization (WHO) Global Tuberculosis Report 2024, an estimated 1.3 million people died from TB in 2023, while approximately one-quarter of the global population harbors latent infection [2]. In Iran, tuberculosis remains a recognized public health concern. According to the

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WHO Global Tuberculosis Report 2024, the estimated incidence is approximately 10 per 100,000 population (range 8.5–13) [3]. Although the overall burden is lower than in some neighboring high-incidence countries, challenges such as delayed diagnosis, limited sensitivity of conventional tests in children, and difficulties in accessing modern molecular diagnostics continue to complicate pediatric TB management. These national data emphasize the need for local evidence from referral centers to better characterize pediatric TB in hospitalized populations. Furthermore, childhood TB is especially difficult to diagnose because of its nonspecific clinical manifestations and the limited sensitivity of conventional diagnostic methods such as the tuberculin skin test (TST) [4]. Although newer diagnostic approaches—including molecular assays such as polymerase chain reaction (PCR) and immune-based assays like interferon-γ release assays (IGRA)—are increasingly available, their routine use in pediatric practice remains limited [5, 6], particularly in Iran, where their availability is largely restricted to referral laboratories due to high costs, limited infrastructure, and unequal distribution of resources across provinces [7].

Young children, particularly those in close contact with infectious adults, are at the highest risk of developing active disease. Evidence shows that most cases of pediatric TB occur soon after exposure, making early detection and prevention crucial [8]. Outcomes of pediatric TB are influenced not only by host factors but also by the pathogen's biology. *M. tuberculosis* evades host immunity through proteins such as early secreted antigenic target 6 kDa (ESAT-6) and culture filtrate protein 10 (CFP-10), and its metabolic plasticity complicates treatment and bacterial clearance [9].

Recent therapeutic advances in pediatric TB management are promising. The WHO 2022 guidelines recommend a shorter, four-month treatment for drug-susceptible non-severe TB in children younger than 16 years. Data from the SHINE trial (Shorter Treatment for Minimal Tuberculosis in Children) demonstrated outcomes comparable to the traditional six-month treatment, with additional benefits in cost reduction and treatment adherence [10, 11]. Shorter all-oral regimens incorporating key agents like bedaquiline and linezolid are increasingly being adopted for drug-resistant TB [12].

Despite these advances, clinical outcomes in pediatric TB remain highly heterogeneous. Key determinants include age, nutritional status, HIV co-infection, and delayed or limited access to care [13, 14].

While several reports from high-burden countries describe hospitalized pediatric TB, comprehensive data from Iranian referral centers remain scarce. This gap limits understanding of disease severity, in-hospital outcomes, and prognostic factors in this patient population. Therefore, we conducted this study to assess the short-term outcomes of hospitalized children with tuberculosis and to identify clinical, demographic, and radiologic variables associated with these outcomes.

MATERIAL AND METHODS

Study design and population. This was a retrospective cohort study including all consecutive children diagnosed with TB and hospitalized at the Pediatric Infectious Diseases Ward, Children's Medical Center, Tehran, Iran, from January 2016 to December 2021. Indications for admission included respiratory distress, clinical instability, or toxic appearance.

Eligibility and case ascertainment. Children were diagnosed with TB by a pediatric infectious diseases subspecialist based on clinical symptoms, exposure history, radiologic findings, and laboratory results.

Case definition. Because this was a retrospective review, case classification relied on the documentation and final diagnoses recorded by a pediatric infectious diseases subspecialist during hospitalization. In clinical practice, diagnostic assessment followed the WHO criteria for pediatric tuberculosis.

Confirmed TB. Bacteriologically confirmed disease, identified by a positive culture, smear, or PCR for *M. tuberculosis*.

Probable TB. Diagnosis required at least three of the following criteria: (i) a history of close contact with an infectious TB case, (ii) clinical features consistent with TB, (iii) a positive immunologic test (TST or IGRA), and (iv) chest radiograph findings typical of tuberculosis.

Possible TB. Cases not meeting the full diagnostic criteria but treated empirically based on the clinical judgment of the pediatric infectious diseases subspecialists [15]. All hospitalized children who met criteria for confirmed or probable TB were included in the final analysis; no patients met the case definition for possible TB during the study period. All 30 eligible admissions had complete clinical and demographic records; therefore, no cases were excluded. When necessary, families were contacted by telephone using contact details documented in the medical records.

Data collection and variables. Demographic information (sex, age, weight, residence, nationality), clinical manifestations, radiologic findings, and laboratory results—including immunologic and molecular assays as well as hematologic/inflammatory indices [white blood cell (WBC) count, hemoglobin (Hb), platelet count (PLT), erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP)]—were abstracted using a structured checklist, along with treatment regimens and in-hospital outcomes. Because not all diagnostic tests were performed in every patient, positivity rates were calculated using the number of patients tested as the denominator (we also report cohort-level proportions, N=30). All 30 patients had complete clinical and demographic data. Specifically, IGRA was available only for a subset of children due to age

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restrictions and limited access, and drug susceptibility testing (DST) was not performed during the study period. Similarly, culture results were unavailable for some cases.

Missing laboratory data were not imputed, and all analyses were conducted using the available dataset for each variable.

Diagnostic methods. PCR testing for *M. tuberculosis* was performed using the Xpert MTB/RIF assay (Cepheid, USA), targeting the *rpoB* gene for rapid molecular confirmation of the *M. tuberculosis* complex. Mycobacterial culture was conducted on Löwenstein–Jensen (LJ) solid medium according to national tuberculosis laboratory protocols and incubated for up to 8 weeks. In selected cases, specimens were referred to reference laboratories for liquid culture using the MGIT 960 system (BD, USA). Acid-fast bacilli (AFB) smears were examined using Ziehl–Neelsen staining. Interferon-γ release assay (IGRA) was performed for a subset of patients using the QuantiFERON-TB Gold Plus test (Qiagen, Germany) when available.

Outcomes. The primary outcome was in-hospital status (recovery or death).

Clinical variables. Baseline clinical characteristics were recorded, including the site of tuberculosis involvement (pulmonary *vs.* extrapulmonary: bone, central nervous system, abdominal, spinal). In this study, pleural complications (such as pleural effusion or empyema) were classified as pulmonary or intrathoracic tuberculosis to maintain consistency with standard anatomical TB classification schemes (intrathoracic *vs.* extrathoracic). These variables were summarized descriptively and, where appropriate, evaluated as potential predictors of in-hospital mortality.

Statistical analysis. Analyses were performed using IBM SPSS Statistics version 26 (IBM Corp., Armonk, NY, USA). Quantitative variables were presented as mean ± standard deviation (SD), and categorical variables as frequency and percentage [n (%)]. Associations between in-hospital mortality and sex, age group, residence, nationality, and site of TB were assessed using Fisher's exact test. Two-sided *P*-values < 0.05 were considered statistically significant.

RESULTS

Patient demographics and baseline characteristics. Thirty hospitalized children met inclusion criteria (girls 16/30, 53.3%; boys 14/30, 46.7%). Mean age was 8.8 ± 3.8 years. Most were aged 10–14 years (18/30, 60.0%), resided in urban areas (21/30, 70.0%), and were Iranian nationals (22/30, 73.3%) (Table 1).

All 30 patients were admitted to the Pediatric Infectious Diseases Ward, and medical record review revealed no documented primary or secondary immunodeficiency, chronic comorbid conditions, or HIV infection. The mean length of hospital stay was 17.6 ± 15.2 days, with a median of 15.5 days (range 3–90 days).

Clinical presentation. Cough (46.7%) was the most frequent symptom, followed by fever (40.0%) and dyspnea (13.3%). Other symptoms included headache (10.0%), hemoptysis (6.7%), seizure (3.3%), and back pain (3.3%) (Table 1).

Radiologic findings. Pulmonary TB occurred in 20/30 (66.7%), and extrapulmonary TB occurred in 10/30 (33.3%) including bone (n: 5), CNS involvement (tuberculous meningitis) (n: 3), abdominal (n: 1), and spinal (n: 1). On chest radiography, consolidation/infiltrate (10/30, 33.3%) and pleural effusion (7/30, 23.3%) were most frequent; hilar lymphadenopathy (4/30, 13.3%), empyema (3/30, 10.0%), bronchiectasis (3/30, 10.0%), and pulmonary fibrosis (1/30, 3.3%) were also observed (Table 1).

Laboratory parameters. Laboratory indices are summarized in Table 1. WBC, hemoglobin, and platelet count were reported as mean ± SD, whereas ESR and CRP, due to non-normal distribution, were reported as median (IQR), consistent with Table 1: ESR 40 (20–65) mm/h; CRP 32 (15–55) mg/L. Due to the limited sample size (only 3 deaths) and incomplete laboratory data for subgroup analysis, statistical comparison of laboratory values between recovered and deceased patients was not feasible.

Diagnostic test performance. Diagnostic investigations were not performed uniformly in all patients. Among those tested, TST was positive in 19/23 (82.6%), IGRA in 5/19 (26.3%), PCR testing across multiple specimen types (sputum/gastric aspirate, tissue biopsy, bronchoalveolar lavage [BAL], cerebrospinal fluid [CSF], synovial fluid) in 18/26 (69.2%), culture from sputum/gastric aspirate in 14/19 (73.7%), and acid-fast bacilli (AFB) smear from sputum/gastric aspirate in 5/19 (26.3%) (Table 2). In the full 30-patient cohort, these correspond to 63.3% (TST), 16.7% (IGRA), 60.0% (PCR), 46.7% (culture), and 16.7% (AFB smear). IGRA was not performed in children younger than 2 years, and test availability limited its use in others. DST was not performed or was unavailable for this cohort; therefore, resistance patterns could not be evaluated.

Among PCR-positive cases (n = 18), specimens yielding positive results were obtained from CSF (n = 3), BAL (n = 6), sputum/gastric aspirate (n = 8), and musculoskeletal specimen (n = 1) (Table 2).

Of the five osseous TB cases, one was molecularly confirmed by PCR testing of tissue specimens, two were supported by histopathology showing necrotizing granulomas consistent with TB, and the remaining two met three out of four clinical criteria (positive contact history, compatible symptoms, suggestive radiologic findings, and positive immunologic test), with clinical improvement following anti-TB therapy.

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Table 1. Baseline demographic, clinical, radiologic, and laboratory characteristics of hospitalized children with tuberculosis (n = 30)

Variable	Category	n (%) or mean ± SD [Median (IQR)]	Notes/normal range
Age group (years)[1]	0–4	3 (10.0)	
	5–9	9 (30.0)	
	10–14	18 (60.0)	
Sex	Female	16 (53.3)	
	Male	14 (46.7)	
Residence	Urban	21 (70.0)	
	Rural	9 (30.0)	
Nationality	Iranian	22 (73.3)	
	Non-Iranian	8 (26.7)	
Clinical manifestations[2]	Cough	14 (46.7)	
	Dyspnea	4 (13.3)	
	Fever	12 (40.0)	
	Headache	3 (10.0)	
	Hemoptysis	2 (6.7)	
	Seizure	1 (3.3)	
	Back pain	1 (3.3)	
	Weight loss/failure to thrive	0 (0.0)	
	Night sweats	0 (0.0)	
	Fatigue/lethargy	0 (0.0)	
Radiologic findings[3]	Consolidation/infiltrate	10 (33.3)	
	Pleural effusion	7 (23.3)	
	Hilar lymphadenopathy	4 (13.3)	
	Empyema	3 (10.0)	
	Bronchiectasis	3 (10.0)	
	Pulmonary fibrosis	1 (3.3)	
Laboratory indices[4]	WBC (×10³/μL)	9.5 ± 4.7	(4–12)
	Hb (g/dL)	11.2 ± 2.1	(11.5–15.5)
	PLT (×10³/μL)	403 ± 174	(150–450)
	ESR (mm/h)	47 ± 41 [40 (20–65)]	<20
	CRP (mg/L)	39 ± 35 [32 (15–55)]	<10

[1]Age groups were defined as 0–4, 5–9, and 10–14 years to ensure mutually exclusive, non-overlapping categories. [2]No constitutional symptoms such as night sweats, weight loss, or fatigue/lethargy were documented in available medical records. [3]A single patient could have more than one radiologic finding; therefore, percentages were not total 100%. [4] Laboratory values for ESR and CRP are presented as mean ± SD along with median (interquartile range, IQR); median (IQR) is reported as the preferred measure of central tendency due to their non-normal distribution. *Abbreviations:* WBC, white blood cells; Hb, hemoglobin; PLT, platelet count; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein.

Table 2. Diagnostic test results (reported both among tested and overall)

Test	Positive/tested	% (among tested)	Overall % (N=30)	Tested/total
TST*	19/23	82.6	63.3	23/30
IGRA**	5/19	26.3	16.7	19/30
PCR (sputum/gastric aspirate, tissue biopsy, BAL, CSF)	18/26	69.2	60.0	26/30
Culture (sputum/gastric aspirate)	14/19	73.7	46.7	19/30
AFB smear (sputum/gastric aspirate)	5/19	26.3	16.7	19/30

*TST was performed using Purified Protein Derivative (PPD, 5 TU).

** IGRA was not performed in children younger than 2 years and was limited by availability. Percentages are reported both among those tested and overall (denominator = 30). *Abbreviations:* TST, tuberculin skin test; IGRA, interferon-gamma release assay; PCR, polymerase chain reaction; BAL, bronchoalveolar lavage; CSF, cerebrospinal fluid; AFB, acid-fast bacilli.

Treatment and clinical outcomes. All patients received standard four-drug anti-TB therapy during hospitalization. Of three patients with tuberculous meningitis, two survived after prolonged hospitalization and were discharged on a reduced two-drug regimen, while the third patient died despite receiving standard therapy. Other survivors were discharged on four-drug therapy.

Overall, 27/30 (90.0%) recovered and 3/30 (10.0%) died during hospitalization. Deaths included a 10-year-old boy with CNS involvement and computed tomography (CT) evidence of possible thalamic abscess or hydrocephalus; a 13-year-old boy with severe pleural effusion and respiratory distress; and an 11-year-old non-Iranian girl with empyema and pleural effusion. Although the two cases with severe pleural disease were classified as pulmonary TB, the fatal outcomes were

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primarily related to the severity of pleural disease rather than lung parenchymal involvement.

Factors associated with in-hospital mortality. No statistically significant differences in in-hospital mortality were detected by sex ($P = 0.586$), age group ($P = 0.667$), residence ($P = 0.998$), nationality ($P = 0.999$), or TB site (pulmonary *vs.* extrapulmonary, $P = 0.251$) (Table 3).

Table 3. In-hospital mortality by baseline characteristics (N = 30)

Variable	Cured n (%)	Died n (%)	Total n	*P*-value[a]
Sex				0.586
Female	15 (93.8)	1 (6.2)	16	
Male	12 (85.7)	2 (14.3)	14	
Age group (years)				0.667
0–4	3 (100.0)	0 (0.0)	3	
5–9	9 (100.0)	0 (0.0)	9	
10–14	15 (83.3)	3 (16.7)	18	
Residence				0.998
Urban	19 (90.5)	2 (9.5)	21	
Rural	8 (88.9)	1 (11.1)	9	
Nationality				0.999
Iranian	20 (90.9)	2 (9.1)	22	
Non-Iranian	7 (87.5)	1 (12.5)	8	
Site of disease				0.251
Pulmonary	18 (90.0)	2 (10.0)	20	
Extrapulmonary	9 (90.0)	1 (10.0)	10	

*According to Fisher's exact test.

Note: Two deaths classified under the "pulmonary TB" group were due to severe pleural complications (one with massive pleural effusion and one with empyema). No deaths occurred among patients with uncomplicated pulmonary TB.

Due to the limited sample size (only 3 deaths) and incomplete laboratory data for subgroup analysis, statistical comparison of laboratory values between recovered and deceased patients was not performed.

DISCUSSION

In this study of children hospitalized with tuberculosis in a tertiary pediatric hospital, most (60.0%) were aged 10–14 years. There were 16 female and 14 male participants. Childhood TB, despite variable global sex distribution, has been reported as either female-predominant or approaching gender parity in our region in prior studies [16-18].

Pulmonary TB was more common (66.7%) than extrapulmonary TB (33.3%), consistent with findings from Iranian, Indian, and Turkish cohorts. Extrapulmonary manifestations included bone, spinal, and central nervous system (CNS) involvement, underscoring both the clinical heterogeneity and diagnostic challenges of hospitalized pediatric TB. Although relatively uncommon, CNS TB is associated with high morbidity and mortality [19-21].

The most common presenting symptom was cough (46.7%), followed by fever (40.0%) and dyspnea (13.3%). The presence of dyspnea generally indicates more extensive pulmonary involvement or pleural complications and therefore reflects more severe disease. Hemoptysis, seizures, and back pain, although rare, were suggestive of more serious or extrapulmonary manifestations. These findings underline the need for pediatricians in high-burden settings to remain vigilant, as nonspecific presentations may easily lead to delayed diagnosis, particularly in resource-limited regions [22-24].

Chest radiography commonly revealed consolidations or infiltrates and pleural effusion. Pleural effusion was observed in 23.3% of our cohort, a rate comparable to previous pediatric TB studies [25]. This consistency supports the accuracy of our radiographic assessment and highlights pleural involvement as a clinically significant and relatively frequent finding in hospitalized children with TB.

While these findings are well recognized, their nonspecific nature in children emphasizes the need for adjunctive diagnostic tools in daily practice. In countries such as Iran, where pediatric TB cases occur, incorporating CT or ultrasonography could support early detection of lymphadenopathy, effusions, and CNS involvement [26].

TST positivity was observed in 19/23 tested children (82.6%), whereas IGRA was positive in 5/19 tested children (26.3%), highlighting IGRA's well-recognized

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limitations in immunocompromised or young children. In our cohort, only three children (10%) were younger than five years, and none had documented immunodeficiency; therefore, the low IGRA positivity rate cannot be fully explained by age or immune status. Limited test availability and the known variability of IGRA performance in pediatric populations may have contributed to this finding. PCR was positive in 18/26 tested children (69.2%), consistent with previous pediatric studies reporting diagnostic yields between 55% and 75%, depending on assay type and sample processing methods [27-29].

Treatment outcomes were encouraging, with 90.0% recovery following standard four-drug therapy. The 10.0% overall mortality observed in this cohort underscores the vulnerability of children with severe disease, as all fatalities occurred among patients with CNS TB and severe pleural complications. Our observed mortality rate of 10% is at the upper limit of the 0.8–10% range previously reported in hospitalized pediatric TB cohorts from Iran, Nigeria, Ethiopia, and Pakistan [30-33].

In this study, no statistically significant differences in in-hospital mortality were observed by sex, age group, nationality, or site of TB. Although one of the three deaths occurred in a non-Iranian child, this difference was not statistically significant. Therefore, our data do not indicate worse outcomes among migrant or refugee children. However, given global evidence showing that displaced populations often face additional risks due to malnutrition, incomplete vaccination, and limited healthcare access, this remains an important area for future investigation in larger cohorts. This finding has direct relevance for public health strategies in countries hosting large refugee populations, including Iran [34].

In our cohort, diagnostic yield varied across modalities. TST showed a high positivity rate, but PCR provided the most consistent diagnostic confirmation across multiple sample types, especially cerebrospinal fluid (CSF) and bronchoalveolar lavage (BAL). These results emphasize that strengthening access to molecular diagnostics—even in individual referral centers—could meaningfully improve pediatric TB care in similar health systems. Inflammatory markers, including ESR and CRP, demonstrated wide interindividual variability, reflecting the typically skewed distribution observed in infectious and inflammatory conditions. Because the data were not normally distributed, median and interquartile range (IQR) values were reported as more robust indicators of central tendency rather than means, providing a more accurate representation of these parameters in the study population.

Although inflammatory markers such as ESR and CRP were recorded, subgroup comparisons stratified by outcome were not possible due to the small number of deaths. Future studies with larger cohorts are required to clarify whether elevated ESR or CRP levels predict poor outcomes.

Overall, this study contributes local data to the limited literature on hospitalized pediatric TB in the region. Although constrained by its retrospective design and small sample size, the findings highlight the diagnostic value of PCR and the need for targeted attention to vulnerable groups, particularly children with CNS involvement and migrant or refugee children.

Multicenter collaborations and prospective studies are essential to validate these findings and inform equitable, child-centered TB programs in high-burden countries.

A major limitation of this study is the lack of DST data (Data in Science Technologies), which precluded assessment of resistance patterns and limited the interpretation of treatment outcomes and mortality.

Among hospitalized children, TB often presented with nonspecific symptoms, leading to delayed diagnosis. Our findings indicate that PCR and mycobacterial culture are currently the most useful diagnostic tools in tertiary pediatric centers, whereas IGRA has limited utility in this population. Standard four-drug therapy achieved favorable recovery in most patients; however, mortality clustered among children with CNS TB and severe pleural disease. Although no statistically significant difference in mortality was observed between Iranian and non-Iranian children in this cohort, vulnerable populations such as migrants should remain a focus of public health attention. Future multicenter studies across the region are needed to clarify long-term outcomes and resistance patterns, and inform national and regional policies for child-focused TB care.

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CONFLICTS OF INTEREST

The authors declare that there are no conflicts of interest associated with this manuscript.

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AI DISCLOSURE

ChatGPT (OpenAI, San Francisco, CA, USA) was used solely for AI-assisted language editing and grammatical refinement. The authors reviewed and approved the final version for accuracy.

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DATA AVAILABILITY

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

AUTHORS' CONTRIBUTIONS

MK: Conceived and designed the study, provided overall supervision, critically revised the manuscript, and had final responsibility for the decision to submit; RS: Conceived and designed the study; ZG: Collected data; MS: Collected data and critically revised the manuscript; AT: Drafted the initial manuscript. All authors read and approved the final manuscript.

ETHICS STATEMENT

This retrospective study was conducted in accordance with the Declaration of Helsinki and was approved by the Ethics Committee of Tehran University of Medical Sciences (Approval ID: IR.TUMS.CHMC.REC.1400.123). The study was primarily a retrospective review of existing hospital medical records. In a very small number of cases (<5), brief telephone contact was made with families exclusively to confirm missing demographic details already documented in the hospital charts; no new clinical or sensitive data were collected, and no physical examination or therapeutic intervention occurred. Because of the retrospective nature of the study and the absence of any intervention or collection of additional personal data, the Ethics Committee formally waived the requirement for written informed consent.

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